

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re the application of: Peter Martin Fischer, et al.

Serial No.: not assigned

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For: Transport Vectors

Attorney Docket No.: CCI-010DV

Box Patent Application  
Commissioner for Patents  
Washington, D.C. 20231

**PRELIMINARY AMENDMENT**

Preliminary to the examination of the above-referenced patent application, please amend the application as follows.

**In the Claims**

Please amend the claim1 and add claims 47-71 as follows.

1. A membrane translocation peptide carrier moiety comprising of formula;

RRMKWKK (SEQ ID NO: 2)

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wherein at least one amino acid residue is deleted from the amino terminus, or variants thereof.

47. A carrier moiety according to claim 1, wherein

- (a) one or more amino acid residues are replaced by a naturally or non-naturally occurring amino acid residue;
- (b) one or more amino acid residues are reversed;
- (c) both (a) and (b) are present together;
- (d) a spacer group is present between any two amino acid residues;
- (e) one or more amino acid residues are in peptoid form;

(f) the (N-C-C) backbone of one or more amino acid residues of the peptide has been modified; or

(g) any of (a)-(f) in combination.

48. A carrier moiety according to claim 47, selected from the group consisting of: KRMKWKK (SEQ ID No. 9), RKMKWKK (SEQ ID No. 10), RREKWKK (SEQ ID No. 11), RRQKWKK (SEQ ID No. 12), RROKWKK (SEQ ID No. 4), RRMKQKK (SEQ ID No. 13), RRMKWFK (SEQ ID No. 14), RORKWKK (SEQ ID No. 15), RRMWKKK (SEQ ID No. 16), RROWKKK (SEQ ID No. 5), RRMKKWK (SEQ ID No. 17) and RROKKWK (SEQ ID No. 18).

49. A carrier moiety according to claim 1, wherein one or more amino acid residues are replaced by homologous replacement.

50. A carrier moiety according to claim 49, wherein the homologous replacement is selected from the group consisting of basic for basic, acidic for acidic, polar for polar, nonpolar for nonpolar, hydrophobic for hydrophobic, hydrophilic for hydrophilic, and amphipathic for amphipathic amino acid replacement.

51. A carrier moiety according to claim 1, wherein one or more amino acid residues are replaced by non-homologous replacement.

52. A carrier moiety according to any of claims 47 to 51, wherein

(a) H, K, and R are basic amino acids;

(b) D and E are acidic amino acids;

(c) A, F, G, I, L, M, P, V and W are non-polar amino acids; and

(d) C, N, Q, S, T and Y are polar amino acids.

53. A carrier moiety according to any of claims 47 to 51, wherein the replacement amino acid is a non-natural selected from the group consisting of: alpha\* and alpha-disubstituted\* amino acids, N-alkyl amino acids\*, lactic acid\*, halide derivatives of natural amino acids such as trifluorotyrosine\*, p-Cl-phenylalanine\*, p-Br-phenylalanine\*, p-I-phenylalanine\*, L-allyl-

glycine\*,  $\beta$ -alanine\*, L- $\alpha$ -amino butyric acid\*, L- $\gamma$ -amino butyric acid\*, L- $\alpha$ -amino isobutyric acid\*, L- $\epsilon$ -amino caproic acid<sup>#</sup>, 7-amino heptanoic acid\*, L-methionine sulfone<sup>##</sup>, L-norleucine\*, L-norvaline\*, p-nitro-L-phenylalanine\*, L-hydroxyproline<sup>#</sup>, L-thioprolin\*, methyl derivatives of phenylalanine (Phe) such as 4-methyl-Phe\*, pentamethyl-Phe\*, L-Phe (4-amino)<sup>#</sup>, L-Tyr (methyl)\*, L-Phe (4-isopropyl)\*, L-Tic (1,2,3,4-tetrahydroisoquinoline-3-carboxyl acid)\*, L-diaminopropionic acid <sup>#</sup> and L-Phe (4-benzyl)\*, wherein the notation \* indicates the hydrophobic nature of the derivative, the notation # indicates the hydrophilic nature of the derivative, and the notation ## indicates amphipathic characteristics.

54. A carrier moiety according to claim 1, wherein the second and third amino acids from the C-terminal end of the peptide are reversed.

55. A carrier moiety according to claim 1, wherein a spacer group is present between any two amino acid residues, and the spacer group is an alkyl group.

56. A carrier moiety according to claim 55, wherein the alkyl group is selected from the group consisting of methyl, ethyl and propyl groups.

57. A carrier moiety according to claim 1, wherein a spacer group is present between any two amino acid residues, and the spacer group is an amino acid residue.

58. A carrier moiety according to claim 57, wherein the spacer group is selected from the group consisting of glycine or  $\beta$ -alanine.

59. A carrier moiety according to claim 1, wherein one or more amino acids are in peptoid form.

60. A carrier moiety according to claim 1, wherein one or more amino acid residues at any of positions 1, 2, 3, 5 or 6 are replaced by a naturally or non-naturally occurring amino acid.

61. A carrier moiety according to claim 1, wherein one or more amino acid residues at any of

positions 1, 2, 3, 5 or 6 are reversed.

62. A carrier moiety according to claims 60, wherein the amino acid residue at position 3 or 7 is replaced.

63. A carrier moiety according to claim 60, wherein the amino acid residue at position 3 is replaced.

64. A carrier moiety according to claim 61, wherein the amino acid residue at position 3 or 7 is reversed.

65. A carrier moiety according to claim 61, wherein the amino acid residue at position 3 is reversed.

66. A carrier moiety according to claims 49 or 50 wherein homologous replacement occurs at any of positions 1 and 2.

67. A carrier moiety according to claims 51 or 53, wherein non-homologous replacement occurs at any of positions 3, 4, 5 and 6.

68. A carrier moiety according to claims 49, 50, 51, or 52, wherein more than one amino acid residue is replaced by homologous or non-homologous replacement.

69. A carrier moiety according to claim 68, wherein amino acid residues at positions 2 and 3 are replaced.

70. A carrier moiety according to claim 68, wherein amino acid residues at positions 4 and 5 are replaced.

71. A carrier moiety according to claim 68, wherein amino acid residues at position 5 and 6 are replaced.

## REMARKS

It is respectfully submitted that this application is in condition for allowance. If a telephone conversation with Applicant's Attorney would expedite the prosecution of the above-identified application, the Examiner is urged to call Applicant's Attorney at (617) 227-7400.

Respectfully submitted,

  
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**VERSION WITH MARKINGS TO SHOW CHANGES MADE**

**In the claims:**

1. (Amended) A membrane translocation peptide carrier moiety comprising the formula:

~~RQIKIWFQNRRMKWKK~~ (SEQ ID No.1)

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RRMKWKK (SEQ ID NO: 2)

1—————7

wherein at least one amino acid residue is deleted from the amino terminus, or variants thereof.